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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Michael Caplan

Serial No.: 09/247,406

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Filed: February 10, 1999

Examiner:

For:

*METHOD FOR ALTERING UNDESIRABLE IMMUNE RESPONSES TO
POLYPEPTIDES*

TECH CENTER 1600/2900

Assistant Commissioner for Patents
Washington, D.C. 20231

INFORMATION DISCLOSURE STATEMENT

Sir:

Pursuant to 37 C.F.R. §1.56 and 37 C.F.R. §1.97, Applicant submits an Information Disclosure Statement, including seven (7) pages of Form PTO-1449 and copies of the documents cited therein.

This Information Disclosure Statement is being filed under 37 C.F.R. § 1.97(b) prior to a first Office Action on the merits. It therefore is believed that no fee is required with this submission. However, should a fee be required, the Commissioner is hereby authorized to charge any required fees to Deposit Account No. 01-2507. A duplicate of this transmittal is enclosed to facilitate the process.

Publications

ABBAS, et al., Cellular and Molecular Immunology (W.B. Saunders Co., Philadelphia, 1994).

BABAKHIN, et al., "Modified allergen immunotherapy: effect on Immunoglobin E production," *Allergy Proc.* 16:195-202 (1995).

BARBAS, et al., "Molecular profile of an antibody response to HIV-1 as probed by combinatorial libraries," *J Mol Biol.* 230(3):812-23 (1993).

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TECH CENTER 1600/2900

U.S.S.N.: 09/247,406
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INFORMATION DISCLOSURE STATEMENT

BITTER, Methods in Enzymology, Vol. 153, Chapter 33, pp. 516-544 (Wu and Grossman, eds.), Academic Press:New York 1987.

BRISTOL, et al. "Development of a murine mutant Ras CD8+ CTL peptide epitope variant that possesses enhanced MHC Class I binding and immunogenic properties," *J Immunol.* 160(5):2433-41 (1998).

BURNS, et al., "Random mutagenesis of the sheep Na,K-ATPase alpha1 subunit generating the ouabain-resistant mutant L793P," *J Biol Chem.* 271(27):15879-83 (1996).

CHALFIE, et al., "Green fluorescent protein as a marker for gene expression," *Science.* 263(5148):802-5 (1994).

CHANG, "Engineering for protein secretion in gram-positive bacteria," Methods in Enzymology, Vol. 153, Chapter 32, pp. 507-516, (Wu and Grossman, eds.), Academic Press:New York 1987.

COLIGAN, et al., Current Protocols in Immunology, volume 1, pp. 3.12.1-14, (John Wiley and Sons, 1994).

COLLEN, et al., "Recombinant Staphylokinase variants with altered immunoreactivity I: Construction and characterization," *Circulation* 94:197-206 (1996).

COLLEN, et al., "Recombinant Staphylokinase variants with altered immunoreactivity III: Species variability of antibody binding patterns," *Circulation* 95:455-462 (1997).

COLMAN, "Production of proteins in the milk of transgenic livestock: problems, solutions, and successes," *Am. J. Clin. Nutr.* 63(4): 639S-6455S (1996).

COLMAN, "Production of therapeutic proteins in the milk of transgenic livestock," *Biochem. Soc. Symp.* 63:141-147 (1998).

CORMACK, et al., "FACS-optimized mutants of the green fluorescent protein (GFP)," *Gene.* 173(1 Spec No):33-8 (1996).

DAVIS, et al., Basic Methods in Molecular Biology (Elsevier, New York, 1986).

DAY, "Genetic Modification of Proteins in Food," *Critical Reviews in Food Science and Nutrition* 36(S):S49-S67 (1996).

DEMATTEO, et al., "Immunologic barriers to hepatic adenoviral gene therapy for transplantation," *Transplantation.* 63(2):315-9 (1997).

U.S.S.N.: 09/247,406

Filed: February 10, 1999

INFORMATION DISCLOSURE STATEMENT

DUFFAUD, et al., "Expression and secretion of foreign proteins in *Escherichia coli*," Methods in Enzymology, Vol. 153, Chapters 31, pp.492-507, (Wu and Grossman, eds.), Academic Press:New York 1987.

ENCELL, et al., "Engineering human DNA alkyltransferases for gene therapy using random sequence mutagenesis," *Cancer Res.* 58(5):1013-20 (1998).

ESPANION & NIEMANN, "Methods of production and perspectives for use of transgenic domestic animals," *DTW Dtsch Tierarztl Wochenschr.* 103(8-9):320-8 (1996).

FERREIRA, et al., "Modulation of IgE reactivity of allergens by site-directed mutagenesis: potential use of hypoallergenic variants for immunotherapy," *FASEB J.* 12(2):231-42 (1998).

FUCHS & ASTWOOD, FUCHS, et al., "Ingredients for fat replacement," *Food Tech.* 51:82-87 (1997).

HAKKAART, et al. "Epitope mapping of the house-dust-mite allergen Der p 2 by means of site-directed mutagenesis," *Allergy* 53:165-172 (1998).

HARLOW & LANE, "Antibodies-A Laboratory Manual" (Cold Spring Harbor, 1988).

HSUING, et al., "Expression of bovine growth hormone derivatives in *Escherichia coli* and the use of the derivatives to produce natural sequence growth hormone by cathepsin C cleavage," Methods in Enzymology, Vol. 153, Chapter 24, pp. 390-401 (Wu and Grossman, eds.), Academic Press:New York 1987.

HUI, et al., "Directing ribosomes to a single mRNA species: A method to study ribosomal RNA mutations and their effects on translation of a single messenger in *Escherichia coli*," Methods in Enzymology, Vol. 153, Chapters 27, pp. 432-452 (Wu and Grossman, eds.), Academic Press:New York 1987.

JENNE, et al., "High resolution mapping of the B cell epitopes of staphylokinase in humans using negative selection of a phage-displayed antigen library," *J Immunol.* 161(6):3161-8 (1998).

JESPERS, et al., "Epitope mapping by negative selection of randomized antigen libraries displayed on filamentous phage," *J Mol Biol.* 269(5):704-18 (1997).

JOHNSTONE & THORPE, Immunochemistry in Practice, Third Edition (Blackwell Scientific Publications, Oxford, 1996)

KAWASAKI, et al., "Identification of three core regions essential for protein splicing of the yeast Vma1 protozyme. A random mutagenesis study of the entire Vma1-derived endonuclease sequence," *J Biol Chem.* 272(25):15668-74 (1997).

U.S.S.N.: 09/247,406
Filed: February 10, 1999
INFORMATION DISCLOSURE STATEMENT

KENNEDY, et al., Monoclonal Antibodies (Plenum Press:New York, 1980).

KIM, et al., "An ovalbumin-IL-12 fusion protein is more effective than ovalbumin plus free recombinant IL-12 in inducing a T helper cell type 1-dominated immune response and inhibiting antigen-specific IgE production," *J Immunol.* 158(9):4137-44 (1997).

The 1995 Lab Manual Source Book (Cold Spring Harbor Laboratory Press:NY, 1995).

LANTIN, et al., "Anaphylactoid purpura like vasculitis following fibrinolytic therapy: role of the immune response to streptokinase," *Clin Exp Rheumatol.* 12(4):429-33 (1994).

LIGHT & LERNER, "Random mutagenesis of staphylococcal nuclease and phage display selection," *Bioorg Med Chem.* 3(7):955-67 (1995).

LIN-GOERKE, et al., "PCR-based random mutagenesis using manganese and reduced dNTP concentration," *Biotechniques.* 23(3):409-12 (1997).

LITTLE, et al., "Human antibody libraries in *Escherichia coli*," *J Biotechnol.* 41(2-3):187-95 (1995).

LORENZO & BLASCO, "PCR-based method for the introduction of mutations in genes cloned and expressed in vaccinia virus," *Biotechniques.* 24(2):308-13 (1998).

MILMAN, "Expression plasmid containing the λ P_L promoter and *cI857* repressor," Methods in Enzymology, Vol. 153, Chapters 30, pp. 482-491, (Wu and Grossman, eds.), Academic Press:New York 1987.

NAGAI & THØGERSEN, "Synthesis and sequence-specific proteolysis of hybrid proteins produced in *Escherichia coli*," Methods in Enzymology, Vol. 153, Chapters 23 to 34 (Wu and Grossman, eds.), Academic Press:New York 1987.

OKADA, et al. "Engineering of hypoallergenic mutants of the *Brassica* pollen allergen, Bra r 1, for immunotherapy," *FEBS Lett.* 434:255-260 (1998).

PARENT & DEVREOTES, "Isolation of inactive and G protein-resistant adenylyl cyclase mutants using random mutagenesis," *J Biol Chem.* 270(39):22693-6 (1995).

PARikh & GUENGERICH, "Random mutagenesis by whole-plasmid PCR amplification," *Biotechniques.* 24(3):428-31 (1998).

PICCINI, et al., "Vaccinia virus as an expression vector," Methods in Enzymology, Vol. 153, Chapter 34, pp. 545-563, (Wu and Grossman, eds.), Academic Press:New York 1987.

U.S.S.N.: 09/247,406

Filed: February 10, 1999

INFORMATION DISCLOSURE STATEMENT

POULSEN, et al., "Improvement of specific immunotherapy by human IgG and modified allergens," *Allergy*. 44(4):241-55 (1989).

REMAUT, et al., "Expression of heterologous unfused protein in *Escherichia coli*," Methods in Enzymology, Vol. 153, Chapter 26, pp. 416-431, (Wu and Grossman, eds.), Academic Press:New York 1987.

ROONEY & MOORE, "Antiparallel, intramolecular triplex DNA stimulates homologous recombination in human cells," *Proc. Natl. Acad. Sci. USA* 92: 2141-2144 (1995).

ROSENSCHEIN, et al., "Streptokinase immunogenicity in thrombolytic therapy for acute myocardial infarction," *Isr J Med Sci.* 27(10):541-5 (1991).

SCHNEIDER & BECK, "New expression vectors for identifying and testing signal structures for initiation and termination of transcription," Methods in Enzymology, Vol. 153, Chapter 28, pp. 452-461, (Wu and Grossman, eds.), Academic Press:New York 1987.

SCHONER, et al., "Expression of eukaryotic genes in *Escherichia coli* with a synthetic two-cistron system," Methods in Enzymology, Vol. 153, Chapter 25 (Wu and Grossman, eds.), Academic Press:New York 1987.

SCHUMACHER & MITCHELL, "Inhibition of murine reaginic antibody responses by nasal immunotherapy with modified allergen," *Int Arch Allergy Appl Immunol.* 62(4):382-8 1980.

SEHON, "The immunogenicity of recombinant proteins and of "magic bullets" represents the main obstacle for the effective *In Vivo* targeting of biologic response modifiers (BRMs)," *Targeting of Drugs* 4:59-65 (1994).

SMITH, et al., "Recombinant allergens for immunotherapy: A Der p 2 variant with reduced IgE reactivity retains T-cell epitopes," *J. Allergol Clin. Immunol.* 101:423-425 (1998).

SMITH, et al., "Site-directed mutagenesis of recombinant Der p 2 decreases *in vitro* and *in vivo* reactivity with IgE Ab," *Journal of Allergy and Clinical Immunology* 97:A187 (1996).

SODOYER, et al., "Full-scale 'naive' human antibody repertoires assembled from VH and VL variable regions," *Hum Antibodies*. 8(1):37-42 (1997).

STEINBERGER, et al., "Allergen-specific IgE production of committed B cells from allergic patients in vitro," *J Allergy Clin Immunol.* 96(2):209-18 (1995).

STEINBERGER, et al., "Construction of a combinatorial IgE library from an allergic patient. Isolation and characterization of human IgE Fabs with specificity for the major timothy grass pollen allergen, Phl p 5," *J. Biol. Chem.* 271:10967-10982 (1996).

U.S.S.N.: 09/247,406

Filed: February 10, 1999

INFORMATION DISCLOSURE STATEMENT

STEINBERGER, et al., "Expression in *Escherichia coli* of human IgE antibody fragments with specificity for major timothy grass pollen allergens using the combinatorial library approach," *Int Arch Allergy Immunol.* 113(1-3):258-9 (1997).

STEWARD & STEENSGAARD, "Antibody Affinity: Thermodynamic Aspects and Biological Significance" (CRC Press, 1983).

SUNG, et al., "Short homopeptide leader sequences enhanced production of human proinsulin in *Escherichia coli*," Methods in Enzymology, Vol. 153, Chapter 23 (Wu and Grossman, eds.), Academic Press:New York 1987.

TOMLINSON, et al., "The repertoire of human germline VH sequences reveals about fifty groups of VH segments with different hypervariable loops," *J Mol Biol.* 227(3):776-98 (1992).

UMETSU, et al., "Th1 and Th2 CD4+ Cells in the pathogenesis of allergic diseases," *Proc Soc Exp Biol Med.* 215(1):11-20 (1997).

VALENTA, et al., "The immunoglobulin E-allergen interaction: a target for therapy of type I allergic diseases," *Int Arch Allergy Immunol.* 116(3):167-76 (1998).

WADHWA, et al., "Production of neutralizing granulocyte-macrophage colony-stimulating factor (GM-CSF) antibodies in carcinoma patients following GM-CSF combination therapy," *Clin Exp Immunol.* 104(2):351-8 (1996).

YASHUE, et al., "Hyposensitization to allergic reastion in rDer f 2-sensitized mice by the intranasal administration of a mutant of rDer f 2, C8/119S," *Clin. Exp. Immunol.* 113:1-9 (1998).

ZACCOLO, et al., "An approach to random mutagenesis of DNA using mixtures of triphosphate derivatives of nucleoside analogues," *J Mol Biol.* 255(4):589-603 (1996).

ZILLIOX, et al., "Henoch-Schoenlein purpura due to streptokinase," *J Clin Immunol.* 13(6):415-23 (1993).

ZOLOTUKHIN, et al., "A "humanized" green fluorescent protein cDNA adapted for high-level expression in mammalian cells," *J Virol.* 70(7):4646-54 (1996).

U.S.S.N.: 09/247,406

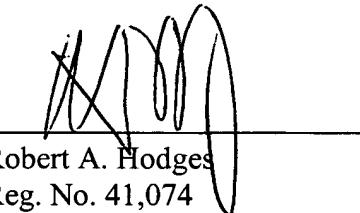
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Remarks

This statement should not be interpreted as a representation that an exhaustive search has been conducted or that no better art exists. Moreover, Applicant invites the Examiner to make an independent evaluation of the cited art to determine its relevance to the subject matter of the present application. Applicant is of the opinion that his claims patentably distinguish over the art referred to herein, either alone or in combination.

Respectfully submitted,



Robert A. Hodges
Reg. No. 41,074

Dated: November 18, 1999

ARNALL GOLDEN & GREGORY, LLP
2800 One Atlantic Center
1201 West Peachtree Street
Atlanta, Georgia 30309-3450
(404) 873-8796
(404) 873-8797 (fax)

U.S.S.N.: 09/247,406

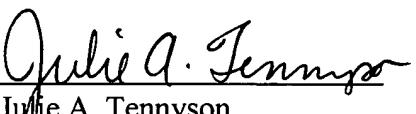
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Certificate of Mailing under 37 C.F.R. § 1.8(a)

I hereby certify that this Information Disclosure Statement, along with any paper referred to as being attached or enclosed, is being deposited with the United States Postal Service on the date shown below with sufficient postage as first-class mail in an envelope addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231.

Date: November 18, 1999


Julie A. Tennyson